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54 **Process for the functionalization of trifluoromethylbenzenes.**

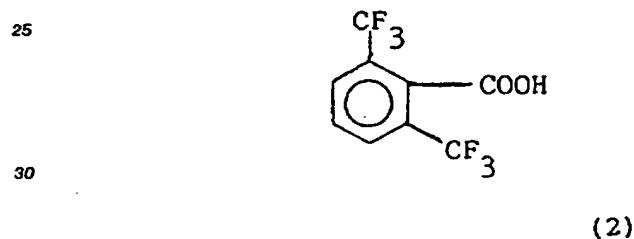
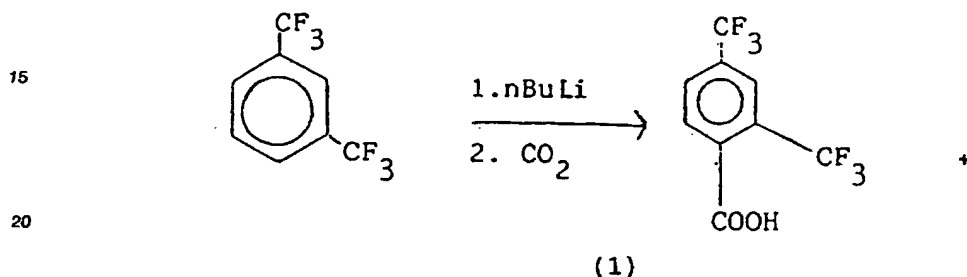
57 Substituted trifluoromethylbenzenes are selectively functionalized by means of an initial metalation of the particular substrate with a metalating agent chosen from mixtures of lithium-and magnesium-alkyls and mixtures of lithium alkyls and magnesium salts and subsequent reaction of the product thus obtained with an electrophile.

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The present invention relates to a process for the selective functionalization of trifluoromethylbenzenes, which comprises the reaction of a specific substrate with a suitable metalating agent and the subsequent reaction of the product thus obtained with an electrophile.

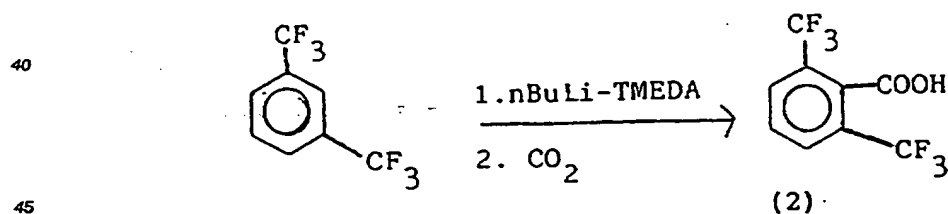
More specifically, the present invention relates to a process for the preparation of substituted trifluoromethylbenzenes, in which the desired substituent enters into a strictly predetermined position and the desired substituted product is formed with high yields and selectivity, in spite of the fact that said substitution competes with other potential substitution reactions.

It is known that 1,3-bis-trifluoromethylbenzene can be transformed into the corresponding benzoic acid by means of initial metalation with lithium alkyls and subsequent reaction with CO_2 . Similarly, from the article in Journal of Organometallic Chemistry (1974), vol. 57, page 321, it can be taken that it is possible to effect the following reaction:



35 wherein the ratio of products (1) and (2) is 60/40.

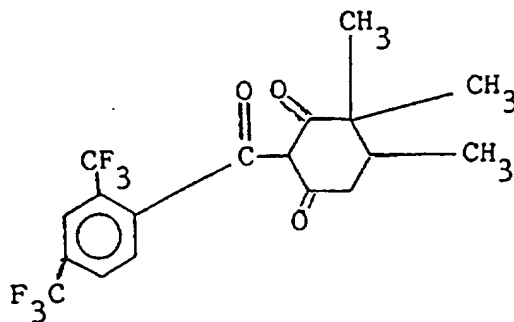
In addition, the article in J. Chem. Soc. (1971), page 3305 describes the following reaction:



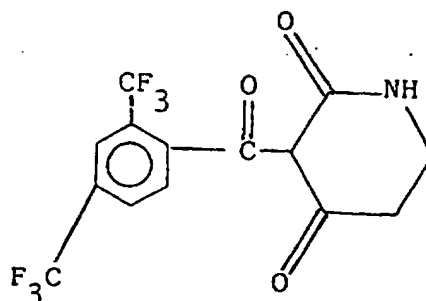
in which the presence of the complexing agent TMEDA (tetramethylethylenediamine) favours the exclusive formation of compound (2).

50 On the other hand, the importance of compound (1) or 2,4-bis-trifluoromethylbenzene derivatives in the preparation of compounds useful in various fields is also well-known.

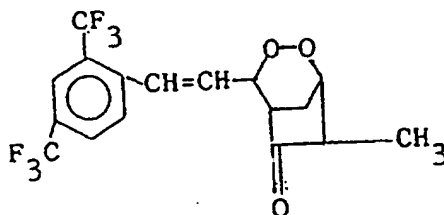
For example, reference can be made to herbicides of formula



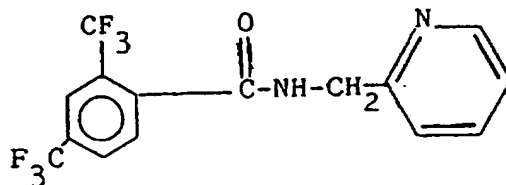
described in EP-A-186 120, or of formula



described in EP-A-278 742; or products used in the pharmaceutical field, for example, in the treatment of malaria, such as that of formula



as described in EP-A-311 955, or in the prevention of coronary disorders, such as that of formula:



as described in US-A-3,946,027.

Other interesting uses of substituted aromatic products belonging to type (1) are found in the dye industry (J. Soc. Dyers Colour. 1982, 98 (1), 10-13), photographic field (JP-A-59/69755), or in the preparation of suitable compounds for the production of apparatus in the non-linear optical industry (JP-A-58/150523).

All previous references, which probably represent only a small part of those existing, make it clear how important it is to have readily available an intermediate of type (1), whereas in fact, as far as is known at the moment, either it cannot be obtained or it can be obtained only in admixture with an undesired product (of

4. Process according to any one of claims 1 to 3, in which the metalation reaction is carried out at a temperature of from -20°C to $+20^{\circ}\text{C}$.
5. Process according to any one of claims 1 to 4, in which the metalation reaction is carried out in the presence of a solvent, preferably selected from tetrahydrofuran, diethyl ether, benzene, toluene, pentane, hexane, heptane, cyclohexane and mixtures thereof.
6. Process according to any one of claims 1 to 5, in which the metalating agent is selected from mixtures of butyllithium and dibutyl magnesium and mixtures of butyllithium and magnesium bromide.
7. Process according to any one of claims 1 to 6, in which the reaction with the electrophilic agent is carried out in the same environment and under the same conditions as the metalation reaction.